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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,267	07/24/2000	ANUSCHIRWAN PEYMAN	02481.1669	2235

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EXAMINER

ZARA, JANE J

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/554,267

Applicant(s)

Peyman ET AL.

Examiner

Jane Zara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26-35, 41-63 is/are pending in the application.
- 4a) Of the above claim(s) 55-62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26-35, 41-54, 63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) ☐ Other: _____

DETAILED ACTION

This office action is in response to the communication filed 9-23-03.

Claims 26-35, 41-63 are pending in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9-23-02 has been entered.

Election/Restrictions

Applicant's election with traverse of 9-22-03 is acknowledged. The traversal is on the ground(s) that sequences 1-58 have already been examined and are not a burden to the examiner since they have already been examined at a prior time. Applicants also argue that the restriction of sequences identical in their nucleotide sequences, but containing various modifications does not place an excessive on the examiner. This is found persuasive partially persuasive. Sequences 21-30 and the corresponding other sequences that contain the same nucleotides but differ only with respect to their modifications (SEQ ID Nos. 2-11 and 40-49) have been examined on their merits as indicated below. Sequences 12-20, 32-39 and 50-58, however, all the

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sequences represent different and distinct nucleotide sequences and are withdrawn from consideration. The data bases required to search the instantly claimed sequences have been growing tremendously in the past few years. As a result, searches are more complicated and time consuming than were in times past. In order to perform an adequate search of each invention, the number of sequences per invention is usually limited now not to ten sequences, but often to a single sequence. Searching more than 10 independent sequences would be too burdensome in this application, since the data bases are so extensive.

The requirement is still deemed proper and is therefore made FINAL.

Claims 55-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. filed 9-23-03.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35 is rejected under 35 U.S.C. 112, first paragraph for lacking enablement over the scope claimed for the reasons of record set forth in the Office action mailed 4-29-01.

No new arguments have been provided for this rejection.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28-35, 41-54 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 28, line 7, it is unclear what "another unit" represents. The metes and bounds of this term cannot be determined. Appropriate clarification is requested.

In claim 28, lines 11-12, it is unclear what "a molecule which adapts the properties of the oligonucleotides to a specific requirement" means. The metes and bounds of this term cannot be determined. Appropriate clarification is requested.

In claim 29, line 2, "one or more modification" is unclear (e.g. perhaps replacing "modification" with —modification—would be remedial).

In claim 29, line 22, it is unclear what "suitable for synthesizing" means (e.g. Does this mean that another unit is to be placed in the oligonucleotide that will then react with such groups as morpholino groups?). Appropriate clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26-29, 32, 33, 35, 41-44, and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Denner et al (WO 94/21664).

Denner et al teach kits, compositions, diagnostic methods and in vitro inhibition of tenascin comprising the administration of oligonucleotides comprising SEQ ID Nos: 22, 23, 24, 26, and their administration to target cells in vitro, whereby the expression of the target gene tenascin is inhibited, and which oligonucleotides optionally further comprise phosphorothioate internucleotide linkages, and which oligonucleotides are made synthetically on a solid phase (See especially sequences listed on pages 9-16; text on page 17, line 9-page 18, line 24; text on page 23, line 24-page 24, line 12; page 36, line 1-31; claims 1-16; also see accompanying sequence alignment data).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26-35, 41-44 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Denner et al in view of Baracchini et al and Friesen et al insofar as the claims are drawn to the particularly claimed antisense oligonucleotides that target tenascin and inhibit its expression in vitro, and which oligonucleotides optionally comprise modified internucleotide linkages, 2'-O- modified sugar and nucleobase residues, 3'-3' or 5'-5' inversions, or conjugation of the oligonucleotide to a polylysine, lipid steroid or lipophilic molecules.

Denner et al teach kits, compositions, diagnostic methods and in vitro inhibition of tenascin comprising the administration of oligonucleotides comprising or consisting of SEQ ID Nos: 22, 23, 24, 26, and their administration to target cells in vitro, whereby the expression of the target gene tenascin is inhibited, and which oligonucleotides optionally further comprise phosphorothioate internucleotide linkages, and which oligonucleotides are made synthetically on a solid phase (See especially sequences listed on pages 9-

16; text on page 17, line 9-page 18, line 24; text on page 23, line 24-page 24, line 12; page 36, line 1-31; claims 1-16; also see accompanying sequence alignment data).

Denner et al do not teach antisense oligonucleotides comprising nucleobase and sugar modifications set forth in the claims including 3'-3' or 5'-5' inversions.

Baracchini et al teach the incorporation of various modifications into antisense oligonucleotides for enhancing cellular uptake, target binding and stability, including an array of sugar (including 2'O-methyl sugars), nucleobase and internucleoside modifications and the conjugation of antisense to various effector molecules. (See entire text, especially column 6 through column 8; claims 1 and 6-10).

Friesen et al teach the incorporation of 3'-3' and 5'-5' inversions into oligonucleotides for increasing their stability (See especially column 3, lines 19-40).

It would have been obvious to one of ordinary skill in the art to design and utilize the oligonucleotide antisense molecules previously taught by Denner et al which target and inhibit the expression of tenascin because the nucleic sequences encoding this particular isoform of tenascin have been taught previously by Denner et al and furthermore Denner et al teach the inhibition of tenascin expression in vitro using antisense comprising SEQ ID NOS: 22, 23, 24 and 26. One of ordinary skill in the art would have been motivated to incorporate nucleobase, sugar and internucleotide linkage modifications into antisense oligonucleotides because such modifications have been shown to increase stability of antisense from nuclease degradation, or to enhance cellular uptake and target binding, as taught previously by Denner et al, Baracchini et al and Friesen.

Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

Claims 45-54 appear free of the prior art searched.

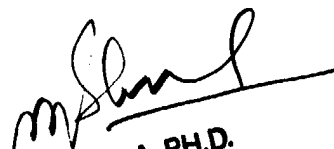
Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

12/14/03


RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

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